

## II. REMARKS

### **Formal Matters**

Claims 1-12 and 15-19 are pending.

Claims 6-8 and 15-19 were examined. Claim 19 is allowed and claims 6-8 and 15-18 are rejected.

The Applicants respectfully request reconsideration of the application in view of the remarks made herein.

### **Withdrawal of rejections**

The Applicants gratefully acknowledge the Examiner's withdrawal of the rejection of claims 6-8 and 15-18 under 35 U.S.C. §103 over Kourilsky (BBRC (1970) 41:1080-1087) in view of Guo (Nucl. Acids Res. (1994) 22:5456-5465).

### **Rejection under 35 U.S.C § 103**

The Office Action stated that claims 6-8 and 15-18 are rejected under 35 U.S.C § 103 as obvious over Kourilsky (Biochimie (1977) 53:1111-1114) in view of Brenner (USPN 5,604,097). Specifically, the Office Action asserts one of skill in the art would incorporate Kourilsky's urea-based hybridization methods into Brenner's oligonucleotide array methods to provide the claimed invention. The Applicants respectfully traverse the rejection.

The MPEP at §2143.02 states "The prior art can be modified or combined to reject claims as *prima facie* obvious as long as there is a reasonable expectation of success."

Accordingly, only references that can be combined with a reasonable expectation of success can be used to establish a *prima facie* case of obviousness.

The Applicants respectfully submit that Kourilsky, in his discussion, explicitly expresses a great deal of doubt about the applicability of his findings (relating to the hybridization behavior of surface bound bacteriophage lambda DNA) to other nucleic acids. As such, one of skill in the art would not combine Kourilsky's methods with those of Brenner (relating to hybridization of surface-bound *oligonucleotides*) with any reasonable expectation of success. Accordingly, this rejection may be withdrawn. Reasoning supporting this position is set forth below.

Kourilsky demonstrates that urea, if present in a hybridization buffer, can lower the hybridization temperature of lambda DNA that is bound to the surface of a nitrocellulose

membrane. However, despite this success, Kourilsky spends most of his discussion explicitly setting forth his doubt that the hybridization temperature of other DNAs can be lowered in the same way. The Examiner's attention is particularly drawn to paragraph 2 of Kourilsky's discussion, in which Kourilsky states "...**conditions optimal for the hybridization of certain fragments may, in fact, be selective against other fragments**" and "**In certain instances, the specificity of the reaction may be questionable** [17]. **Therefore the above conditions do not necessarily apply to other experimental circumstances**, and may have to be modified accordingly". (Emphasis added). The Applicants respectfully submit that, in view of Kourilsky's doubt, one of skill in the art would have no expectation that Kourilsky's findings could readily be transferred to oligonucleotide methods. In fact, Kourilsky's warnings about selection against certain fragments and questionable reaction specificity would almost certainly point one of skill in the art directly *away* from trying to lower the hybridization temperature of oligonucleotides using urea.

In other words, since Kourilsky's methods involve surface-bound bacteriophage lambda DNA molecules that are much longer than the claimed oligonucleotides, one of skill in the art, in view of Kourilsky's explicit doubt about the applicability of his findings to other types of DNA, would have no reason to expect that urea would lower the hybridization temperature of an oligonucleotide. In fact, in view of Kourilsky's statements, one of skill in the art would undoubtedly conclude that urea-containing buffers for hybridization of oligonucleotides would probably yield poor results, and, as such, are generally avoidable.

In view of the foregoing, the Applicants respectfully submit that this rejection fails to meet the requirements set forth in MPEP §2143.02. Accordingly, this rejection may be withdrawn without any further discussion.

**CONCLUSION**

The Applicants submit that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone Timothy Joyce at (650) 485 4310.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§1.16 and 1.17 that may be required by this paper, or to credit any overpayment, to Deposit Account No. 50-1078.

Respectfully submitted,  
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